

REMARKS

Claims 1-3, 16-27, 38-40, 43, and 48 have been canceled herein. Such cancellation is without prejudice on the merits.

Claims 4, 7, and 41 have been amended herein. These amendments enjoy explicit support in the specification and claims as originally filed. Regarding Claim 4 as amended, see the Sequence List and Claim 36 as originally filed. Claim 7 has been amended solely to make it depend from Claim 4. Claim 41 has been amended to recite that "one and only one" leaving group is covalently bonded to the isolated polypeptide. Throughout the specification and claims, the application refers to isolated polypeptides that contain but one detectable leaving group attached thereto. In no instance does the specification refer to substrates having matched pairs of self-quenching leaving groups attached thereto.

Applicants thank Examiner Celsa for indicating that Claims 4-15, 28-37, 44, and 46-47 contain allowable subject matter. The objection to Claims 14 and 46 is believed to have been addressed; see the following section.

Objection to Claims 14 and 46:

The objection to Claims 14 and 46 is believed to have been overcome by appropriate amendment to independent Claims 4 and 41. As amended, the independent claims now include within their scope the polypeptide PANK as recited in dependent claims 14 and 46. Withdrawal of the rejection is respectfully requested.

Rejection of Claims 41, 42, and 45 Under 35 USC §§102(a) or (b) in View of Wei et al., WO 98/50579:

This rejection is believed to have been overcome by amending Claim 41 to recite that the isolated polypeptide contains "one and only one detectable leaving group is covalently bound to P4-P3-P2-P1." The inclusion of this language draws a clear and insurmountable distinction between the claimed kit and the disclosure of the Wei et al.

publication because in Wei's approach a mated pair of dye "dimers" are required for Wei's protocol to function.

Specifically, Wei et al. describe a self-quenching arrangement wherein the polypeptide substrate includes two mated fluorophores covalently bound to the substrate. See, for example, Wei et al. at page 9, the paragraph starting at line 21. When the two fluorophores are held in such close proximity, they self-quench, and no detectable signal is generated. But when the polypeptide substrate is cleaved by the action of the protease, the fluorophores are physically separated, and can no longer self-quench. When separated in this fashion, the fluorophores then generate detectable signal.

Thus, in Wei et al.'s disclosure, every single embodiment requires the presence of a mated pair of fluorophores. Applicants therefore submit that the amendment to Claim 41 overcomes the rejection under §102 in view of Wei et al. because the positive language of Claim 41 now requires that there be no more than one (1) fluorophore per polypeptide. Wei et al., in contrast, require 2 fluorophores per polypeptide substrate.

Applicants also note that Claim 41 as amended is not obvious in view of the Wei et al. reference because if Wei's approach were modified to arrive at the presently claimed invention, the method described by Wei et al. would not function. The law in this regard is well-settled: there can be no prima facie showing of obviousness if a modification proposed by the Office destroys the utility of the method described in the applied prior art.

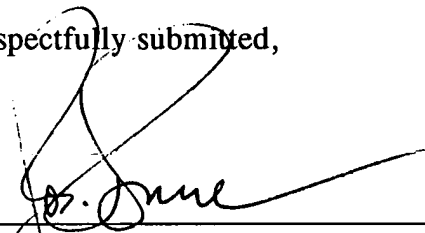
The Wei et al. protocol requires that each polypeptide substrate include a mated pair of fluorophore dyes that self-quench. Claim 41 of the present application, in contrast, requires that the polypeptide substrate contains one and only one fluorophore. There is no technological motivation to move from the two fluorophores taught by Wei et al. to the one fluorophore required in Claim 41 as amended because Wei et al.'s stated approach won't work using only one fluorophore per substrate. Thus, the invention recited in Claim 41 as amended is both novel and unobvious in view of the Wei et al. document.

Withdrawal of the rejection of Claims 41, 42, and 45 under 35 USC §§102(a) or (b) in view of Wei et al. is respectfully requested.

CONCLUSION

Applicants submit that the application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,



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